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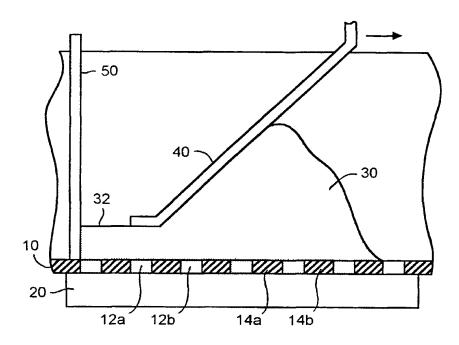
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[Continued on next page]

(54) Title: METHOD AND APPARATUS FOR DISTRIBUTING POWDER



(57) Abstract: There is provided an apparatus for densifying, preparing or levelling powdered medicament which comprises a powder bed (30); and a blade (40) movable relative to the powder bed on a linear path, wherein said blade presents a forward acute angle to said linear path.



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Method and apparatus for distributing powder

Field of invention

This invention relates to a method and apparatus for distributing powder. This invention has particular application to preparing, levelling or densifying a powder bed ready for measuring and removing doses of powdered medicament for transfer to a container such as a blister pocket of a blister pack.

Background to the invention

Powder beds containing a reservoir of excess powder are commonly used in the filling of containers, such as blister pockets, with defined doses of powdered medicament. Prior art filling systems often use a bowl which is either static or rotatable around a central axis. Typically the powder in the bowl is levelled by the use of a blade or other suitable leveller, which is mounted at right angles to the bottom of the bowl. The blade may be rotary if used in a static bowl or is usually fixed if used in a rotating bowl. The levelled powder is then ready for the measuring and removal of the defined doses of powdered medicament from the powder bed and the doses are then transferred to the container.

The use of a blade mounted at right angles to the bottom of the powder bed to distribute the powder throughout the bed may however result in non-uniformity of the density of the levelled bed. This may lead to inaccurate dosing of the powder and additional compaction steps are often required to try and resolve the problem.

The applicants have now found that the use of a blade which is angled at less than 90°, typically less than 60°, improves the density of the powder and therefore reduces the need for an additional compaction stage. As the blade passes through

the powder reservoir it exerts a compressive force on the powder and this increases the uniformity of the density of the powder in the reservoir.

The applicants have also found that the use of a blade which moves on a linear path and which presents a forward acute angle to the powder is preferable to that of a blade which moves on a rotary path through powder in a bowl. The use of the blade movable on a linear path further improves the uniformity of the density of the powder bed and there may also be less powder wastage than with a rotary system. Linear movement of the powder is also more suited to a linear pack or strip and less powder may be required.

Summary of the invention

According to the present invention there is provided an apparatus for densifying, preparing or levelling powdered medicament comprising:

- a) powder bed; and
- b) a blade movable relative to the powder bed on a linear path, wherein said blade presents a forward acute angle to said linear path.

The powdered medicament may comprise drug alone or the drug together with an excipient.

The blade may move across a static powder bed to densify, prepare or level the powder. Alternatively the position of the blade may be fixed while the powder bed is movable.

The forward angle is the angle created between the linear path and the surface of the blade which contacts the powder. The linear path is typically horizontal.

Preferably, said forward acute angle is between 1 and 60°. More preferably, the forward acute angle is between 5 and 25°.

In one aspect the blade has a tail section. The tail section is not co-linear with the rest of the blade. The tail section can be essentially parallel to the linear path, but

preferably the tail section presents a second forward acute angle to the linear path. Preferably, said second forward acute angle is between 3 and 15°.

In another aspect the blade presents multiple forward acute angles to the linear path. Preferably, the blade forms a curve. The multiple forward acute angles are the different angles created between different portions of the curved blade and the linear path. Preferably, the curve has a radius of 20 to 100 mm. The radius is taken from the point that would form the mid point of the circle created if the arc of the curve were extended so that the two ends of the curved blade are joined. Alternatively, the curve may form part of an ellipse.

According to another aspect of the invention the blade is articulated.

Preferably, the powder bed is elongate. Preferably, the powder bed is essentially rectangular and the blade is movable across the length or width of the powder bed.

Preferably, movement of the blade relative to the powder bed exerts a compressive force on said powdered medicament.

Preferably, the blade material is selected from the group consisting of pharmaceutical grade metallic materials and non-metallic materials. The preferred material is pharmaceutical grade stainless steel.

In one aspect the invention further comprises at least one subsequent blade. Preferably, the at least one subsequent blade moves along the powder bed at a lower level than that of the blade. Preferably, the distance between the level of movement of the blade and the at least one subsequent blade is 0 to 12 mm. More Preferably, the distance between the level of movement of the blade and the at least one subsequent blade is 1 to 3 mm. A second subsequent blade would move along the powder bed at a lower level than the first subsequent blade.

Optionally the blade and/or the at least one subsequent blade may have plural movements relative to the powder bed. The number of plural movements can be varied according to the flow properties of the powder and helps to ensure that the

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powder has a uniform density. Passing a blade across the powder bed more than once may in some circumstances be more economical than having multiple blades, although the time taken for the multiple passes may be longer than the time taken for multiple blades to act.

Preferably, the apparatus further comprises powdered medicament located on the powder bed.

Preferably, the powdered medicament comprises a drug. Preferably, the drug is selected from the group consisting of albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof and any mixtures thereof. A particularly preferred combination comprises salmeterol xinafoate and fluticasone propionate.

Preferably, the powdered medicament additionally comprises an excipient. Preferably, the excipient is a sugar. A suitable sugar is lactose.

The invention also provides a method of densifying, preparing or levelling powdered medicament comprising

- a) locating powdered medicament on a powder bed; and
- b) moving a blade relative to said powder bed on a linear path such that said blade moves through the powdered medicament,

wherein the blade presents a forward acute angle to said linear path.

The powdered medicament may comprise drug alone or the drug together with an excipient.

The blade may move across a static powder bed to densify, prepare or level the powder. Alternatively the position of the blade may be fixed while the powder bed is movable.

The forward angle is the angle created between the linear path and the surface of the blade which contacts the powder. The linear path is typically horizontal.

Preferably, the forward acute angle is between 1 and 60 °. More Preferably, said forward acute angle is between 5 and 25°.

In one aspect the blade has a tail section. The tail section is not co-linear with the rest of the blade. The tail section can be essentially parallel to the linear path, but preferably, the tail section presents a second forward acute angle to the linear path. Preferably, said second forward acute angle is between and 3 and 15°.

In another aspect the blade presents multiple forward acute angles to the linear path. Preferably, the blade forms a curve. The multiple forward acute angles are the different angles created between different portions of the curved blade and the linear path. Preferably, the curve has a radius of 20 to 100mm. The radius is taken from the point that would form the mid point of the circle created if the arc of the curve were extended so that the two ends of the curved blade are joined. Alternatively the curve may form part of an ellipse.

In a further aspect of the invention the blade is articulated.

Preferably, the powder bed is elongate. Preferably, the powder bed is essentially rectangular and the blade moves across the length or width of the bed.

Preferably, movement of the blade relative to the powder bed exerts a compressive force on the powdered medicament.

Preferably, the blade material is selected from the group consisting of pharmaceutical grade metallic materials and non-metallic materials. The preferred material is pharmaceutical grade stainless steel.

Preferably, the powder is distributable by at least one subsequent blade. Preferably, the at least one subsequent blade moves along the powder bed at a lower level than that of the blade. Preferably, the distance between the level of movement of the blade and the at least one subsequent blade is 0 to 12 mm. More preferably, the distance between the level of movement of the blade and the at least one

subsequent blade is 1 to 3 mm. A second subsequent blade would move along the powder bed at a lower level than the first subsequent blade.

Optionally the blade and/or the at least one subsequent blade may have plural movements relative to the powder bed. The number of plural movements can be varied according to the flow properties of the powder and helps to ensure that the powder has a uniform density. Passing a blade across the powder bed more than once may in some circumstances be more economical than having multiple blades, although the time taken for the multiple passes may be longer than the time taken for multiple blades to act.

Preferably, the powdered medicament comprises a drug. Preferably, the drug is selected from the group consisting of albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof and any mixtures thereof. A particularly preferred combination comprises salmeterol xinafoate and fluticasone propionate.

Preferably, the powdered medicament additionally comprises an excipient. Preferably, the excipient is a sugar. A suitable sugar is lactose.

According to the invention, the apparatus may be used for densifying, preparing or levelling a sample of powdered medicament.

Brief Description of the Drawings

The invention will now be described with reference to the accompanying drawings in which:

Figure 1 shows an apparatus for densifying, levelling and preparing powdered medicament in accord with the present invention;

Figure 2 shows an alternative apparatus in accord with the present invention;

Figures 3a and 3b show an alternative apparatus in accord with the present invention;

Figure 4 shows a further alternative apparatus in accord with the present invention; and

Figure 5 shows a further alternative apparatus in accord with the present invention.

Detailed Description of the Drawings

Figure 1 shows an apparatus for densifying, levelling and preparing powdered medicament in accord with the present invention. A perforated plate 10 in contact with a blanking plate 20 creates closed-off perforations 12a, 12b. On the opposite side of the perforated plate 10 to the blanking plate 20 is a reservoir of powder 30. The powder 30 comprises a suitable medicament formulation. Situated above the powder reservoir is blade 40 and wiper blade 50. The blade may be seen to have a following tail section.

The blade 40 is shown mounted at an angle of approximately 45° to the perforated plate 10 and depicts one possible configuration of a blade 40 relative to the perforated plate 10 in accord with the present invention. It should be appreciated that the blade 40 may be mounted at any acute angle, typically (but not exclusively) between 1 and 60° and may be varied according to the properties of the powder to optimise powder direction. Examples of other suitable blades are shown in Figures 2 to 5 and described below. The tail section of the blade is not essential to its action. The wiper 50 is shown mounted at an angle of approximately 90° to the perforated plate 10, however effective operation of the wiper 50 can be obtained within a wide range of angles.

The powder 30 is directed into the perforations 12a, 12b by the action of a sweeping blade 40 which moves horizontally across the powder reservoir 30 on a linear path and moves the powder 30 along the length of the perforated plate 10 leaving a thin layer of excess powder 32 still in contact with the perforated plate 10. The blade 40 shown in the figure moves at an angle of approximately 45° to the linear path and acts to compress the powder so that the thin layer of excess powder 32 and the powder in the perforations 12a, 12b are of a more uniform density than before movement of the blade. A wiper blade 50, for example of stainless steel or rubber, follows the sweeping blade 40 and moves along the powder reservoir 30 in close

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proximity to the surface of the perforated plate 10, removing the excess powder 32 from the perforated plate surface 10. Doses of powder are retained in the perforations 12a, 12b after action of the wiper blade and these doses may be transferred to a container, for example a blister pocket of a blister strip.

Figure 2 shows an alternative apparatus as described herein. A perforated plate 110 in contact with a blanking plate 120 creates closed-off perforations 112a, 112b. On the opposite side of the perforated plate 110 to the blanking plate 120 is a reservoir of powder 130. The powder 130 comprises a suitable medicament formulation. Situated above the powder reservoir are blades 140, 142.

The blades 140, 142 are shown with a long tail section and a shorter more upright section. The blades 140, 142 are mounted so that the tail section is at an angle of about 10° relative to the perforated plate 110. The upright sections of the blades 140,142 are not essential to their action. Blade 142 is mounted slightly closer to the perforated plate 110 than blade 140.

The powder 130 is directed into the perforations 112a, 112b by the action of blades 140,142 which move across the powder reservoir 130 on a linear path and move the powder 130 along the length or width of the perforated plate 110. The tail sections of the blades 140, 142 shown in the figure move at an angle of approximately 10° to the linear path and act to compress the powder so that the thin layer of excess powder 132 and the powder in the perforations 112a, 112b are of a more uniform density than before movement of the blade. Movement of the tail sections of the blades 140,142 through the powder have a more compressive effect than movement of the blade shown in Figure 1 due to the smaller angle.

The first blade 140 moves through the powder reservoir 130 leaving a thin layer of excess powder 132 still in contact with the perforated plate 110. The second blade 142 moves across the perforated plate 110 at a lower level than the first blade 140, moving through the thin layer of excess powder 132 and directing powder 130 into any spaces in the perforations 112a, 112b not filled by the action of the first blade 140. The second blade 142 also acts to further compress the powder 130. Additional blades may follow the second blade 142 if required. Alternatively the

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blades 140, 142 may be passed through the powder reservoir 130 more than once if the powder has poor flow properties. The blades 140,142 may then be moved back across the powder reservoir 130 without disrupting the thin layer of excess powder 132, or alternatively turned around ready for travel in the opposite direction so that they are ready for use in the next cycle. A wiper, as shown in Figure 1, may then remove the excess powder from the perforated plate 110 surface.

Figures 3a and 3b show an alternative apparatus described herein. A perforated plate 210 in contact with a blanking plate 220 creates closed-off perforations 212a, 212b. On the opposite side of the perforated plate 210 to the blanking plate 220 is a reservoir of powder 230. The powder 230 comprises a suitable medicament formulation. Situated above the powder reservoir are blades 240, 242.

The blades 240, 242 are similar to the blade shown in Figure 1 however the tail section of the blade is angled. θ and ϕ show the angles of the sections of the blade relative to the linear path. θ is approximately 45° and ϕ is approximately 15°. The angled tail sections pass through the powder after the main section of the blade and have a further compressive effect on the powder, acting to further improve the density of the thin layer of powder 232 left in contact with the perforated plate 210. Figure 3b shows the movement of the second blade 242, following the action of blade 240 and moving at a slightly lower level.

Figure 4 shows a further alternative apparatus as described herein. The powder reservoir 330 is formed on powder bed 317. Any suitable surface or container may be used to hold the powder 330. Mounted above the powder bed 317 are blades 340, 342.

The blades 340 and 342 are similar to those shown in Figures 3a and 3b and move through the powder 330 to create a layer of powder 332 with a more uniform density to that previously on the powder bed. The layer of powder 332 is then ready for the removal of doses of powder 330 for transfer to a container, such as a blister pocket of a blister strip. The doses of powder may be measured and removed by any suitable apparatus known in the art, for example dosating pins.

It should be appreciated that movement of the blades 340, 342 in close proximity to the surface of the powder bed 317 would remove all the powder 330 from the surface of a section of the powder bed 317. The blades 340, 342 may then be moved to the far side of the powder bed 317, turned around and raised slightly so that they can then move back across the powder bed 317 and re-lay the powder 330 to create a new layer of powder 332. This may be particularly appropriate to the situation where doses of powder are removed from the layer of powder 332, creating an uneven surface with holes or gaps.

Figure 5 shows a further alternative apparatus as described herein. The powder reservoir 430 is formed on powder bed 417. Any suitable surface or container may be used to hold the powder 430. Mounted above the powder bed 417 is blade 444.

The blade 444 is curved and the angle at which it moves through the powder bed, relative to the linear path therefore varies along the length of the blade 444. The blade 444 moves through the powder 430 and creates a thin layer of powder 432 with a more uniform density than existed before movement of the blade 444. The layer of powder 432 is then ready for removing doses of powder 430 for transfer to a container such as a blister pocket of a blister strip. The doses of powder may be measured and removed by any suitable apparatus known in the art, for example dosating pins.

It should be appreciated that movement of the blade 444 in close proximity to the surface of the powder bed 417 would remove all the powder from the surface of a section of the powder bed. The blade 444 may then be moved to the far side of the powder bed, turned around and raised slightly so that it can then move back across the powder bed and re-lay the powder to create a new layer of powder. This may be particularly appropriate to the situation where doses of powder 430 are removed from the layer of powder 432, creating an uneven surface with holes or gaps.

The invention is suitable for preparing, levelling and densifying a powder bed ready for measuring and removing doses of powdered medicament for transfer to a

suitable container and is particularly suitable for powdered medicament used in the treatment of respiratory disorders.

Appropriate medicaments may thus be selected from, for example, analgesics, e.g., codeine, dihydromorphine, ergotamine, fentanyl or morphine; anginal preparations, diltiazem; antiallergics, e.g., cromoglycate, ketotifen or nedocromil: antiinfectives e.g., cephalosporins, penicillins, streptomycin, sulphonamides, tetracyclines, zanamivir and pentamidine; antihistamines, e.g., methapyrilene; antie.g., beclomethasone dipropionate, fluticasone propionate, inflammatories, budesonide, rofleponide, mometasone furoate, ciclesonide or flunisolide. triamcinolone acetonide; antitussives, e.g., noscapine; bronchodilators, e.g., albuterol, salmeterol, ephedrine, adrenaline, fenoterol, formoterol, isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, pirbuterol, reproterol, rimiterol. terbutaline. isoetharine. tulobuterol or 4-hydroxy-7-[2-[[2-[[3-(2phenylethoxy)propyl]sulfonyl]ethyl]amino]ethyl-2(3H)-benzothiazolone; e.g., amiloride; anticholinergics, e.g., ipratropium, tiotropium, atropine or oxitropium; hormones, e.g., cortisone, hydrocortisone or prednisolone; xanthines, e.g., aminophylline, choline theophyllinate, lysine theophyllinate or theophylline; therapeutic proteins and peptides, e.g., insulin or glucagon; vaccines, diagnostics, and gene therapies. It will be clear to a person skilled in the art that, where appropriate, the medicaments may be used in the form of salts, (e.g., as alkali metal or amine salts or as acid addition salts) or as esters (e.g., lower alkyl esters) or as solvates (e.g., hydrates) to optimise the activity and/or stability of the medicament and/or to minimise the solubility of the medicament in the propellant.

Preferred medicaments are selected from albuterol, salmeterol, ipratropium bromide, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof, e.g., the sulphate of albuterol and the xinafoate of salmeterol.

Medicaments can also be delivered in combinations. Preferred formulations containing combinations of active ingredients contain salbutamol (e.g., as the free base or the sulphate salt) or salmeterol (e.g., as the xinafoate salt) in combination with an anti-inflammatory steroid such as a beclomethasone ester (e.g., the

dipropionate) or a fluticasone ester (e.g., the propionate). A particularly preferred combination comprises salmeterol xinafoate salt and fluticasone propionate.

It may be appreciated that any of the parts of the apparatus which contact the powder may be coated with materials such as fluoropolymer materials which reduce the tendency of medicament to adhere thereto. Suitable fluoropolymers include polytetrafluoroethylene (PTFE) and fluoroethylene propylene (FEP). Any movable parts may also have coatings applied thereto which enhance their desired movement characteristics. Frictional coatings may therefore be applied to enhance frictional contact and lubricants used to reduce frictional contact as necessary.

It will be understood that the present disclosure is for the purpose of illustration only and the invention extends to modifications, variations and improvements thereto.

The application of which this description and claims form part may be used as a basis for priority in respect of any subsequent application. The claims of such subsequent application may be directed to any feature or combination of features described therein. They may take the form of product, method or use claims or may include, by way of example and without limitation, one or more of the following claims:

Claims

- 1. An apparatus for densifying, preparing or levelling powdered medicament comprising:
- a) a powder bed; and
- b) a blade movable relative to the powder bed on a linear path, wherein said blade presents a forward acute angle to said linear path.
- 2. An apparatus according to claim 1 wherein said forward acute angle is between 1 and 60°.
- 3. An apparatus according to claim 2 wherein the forward acute angle is between 5 and 25°.
- 4. An apparatus according to any of claims 1 to 3 wherein the blade has a tail section.
- 5. An apparatus according to claim 4 wherein said tail section presents a second forward acute angle to the linear path.
- 6. An apparatus according to claim 5 wherein said second forward acute angle is between 3 and 15°.
- 7. An apparatus according to any of claims 1 to 5 wherein the blade presents multiple forward acute angles to the linear path.
- 8. An apparatus according to claim 6 wherein the blade forms a curve.
- 9. An apparatus according to claim 7 wherein the curve has a radius of 20 to 100 mm.
- 10. An apparatus according to any of claims 1 to 8 wherein the blade is articulated.

11. An apparatus according to any of claims 1 to 9 wherein the powder bed is elongate.

- 12. An apparatus according to any of claims 1 to 11 wherein the powder bed is essentially rectangular and the blade is movable across the length or width of the powder bed.
- 13. An apparatus according to any of claims 1 to 12 wherein movement of the blade relative to the powder bed exerts a compressive force on said powdered medicament.
- 14. An apparatus according to any of claims 1 to 13 wherein the blade material is selected from the group consisting of pharmaceutical grade metallic materials and non metallic materials.
- 15. An apparatus according to any of claims 1 to 14 further comprising at least one subsequent blade.
- 16. An apparatus according to claim 15 wherein the at least one subsequent blade moves along the powder bed at a lower level than that of the blade.
- 17. An apparatus according to claim 16 wherein the distance between the level of movement of the blade and the at least one subsequent blade is 0 to 12 mm.
- 18. An apparatus according to claim 17 wherein the distance between the level of movement of the blade and the at least one subsequent blade is 1 to 3 mm.
- 19. An apparatus according to any of claims 1 to 18 further comprising powdered medicament located on the powder bed.
- 20. An apparatus according to claim 19 wherein the powdered medicament comprises a drug.

21. An apparatus according to claim 20 wherein the drug is selected from the group consisting of albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof and any mixtures thereof.

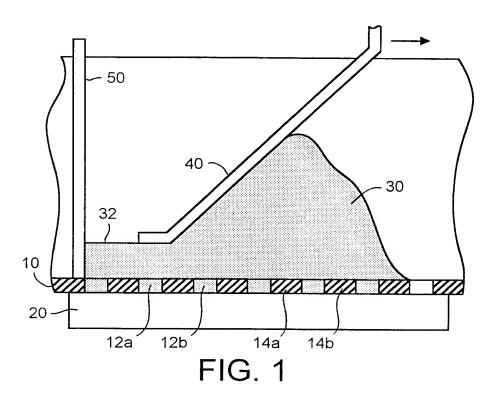
- 22. An apparatus according to either of claims 20 and 21 wherein the powdered medicament additionally comprises an excipient.
- 23. An apparatus according to claim 22 wherein the excipient is a sugar.
- 24. A method of densifying, preparing or levelling powdered medicament comprising
- a) locating powdered medicament on a powder bed; and
- b) moving a blade relative to said powder bed on a linear path such that said blade moves through the powdered medicament, wherein the blade presents a forward acute angle to said linear path.
- 25. A method according to claim 24 wherein the forward acute angle is between 1 and 60 °.
- 26. A method according to claim 25 wherein said forward acute angle is between 5 and 25°.
- 27. A method according to any of claims 24 to 26 wherein the blade has a tail section.
- 28. A method according to claim 27 wherein said tail section presents a second forward acute angle to the linear path.
- 29. A method according to claim 28 wherein said second forward acute angle is between and 3 and 15°.

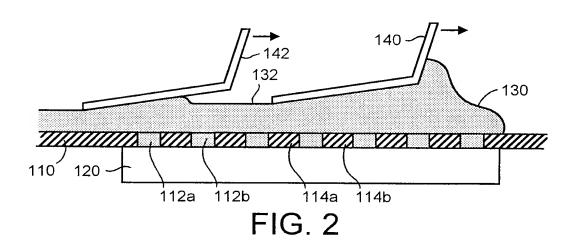
30. A method according to any of claims 24 to 29 wherein the blade presents multiple forward acute angles to the linear path.

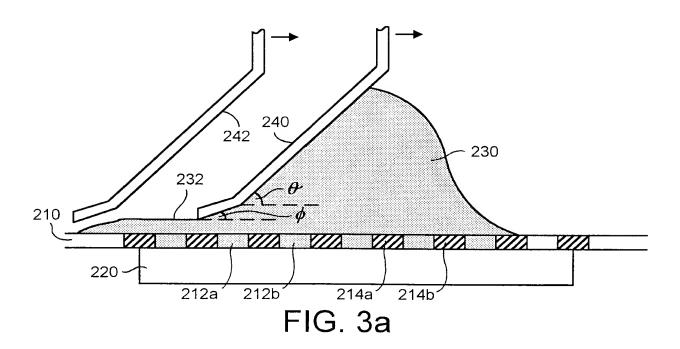
- 31. A method according to claim 30 wherein the blade forms a curve.
- 32. A method according to claim 31 wherein the curve has a radius of 20 to 100mm.
- 33. A method according to any of claims 24 to 32 wherein the blade is articulated.
- 34. A method according to any of claims 24 to 33 wherein the powder bed is elongate.
- 35. A method according to any of claims 24 to 34 wherein the powder bed is essentially rectangular and the blade moves across the length or width of the bed.
- 36. A method according to any of claims 24 to 35 wherein movement of the blade relative to the powder bed exerts a compressive force on the powdered medicament.
- 37. A method according to any of claims 24 to 36 wherein the blade material is selected from the group consisting of pharmaceutical grade metallic materials and non metallic materials.
- 38. A method according to any of claims 24 to 37 wherein the powder is distributable by at least one subsequent blade.
- 39. A method according to claim 38 wherein the at least one subsequent blade moves along the powder bed at a lower level than that of the blade.
- 40. A method according to claim 39 wherein the distance between the level of movement of the blade and the at least one subsequent blade is 0 to 12 mm.
- 41. A method according to claim 40 wherein the distance between the level of movement of the blade and the at least one subsequent blade is 1 to 3 mm.

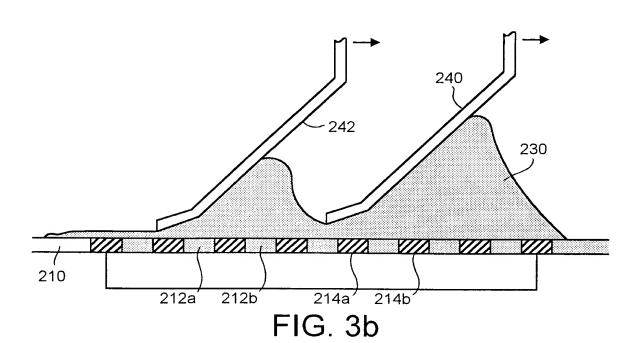
42. A method according to any of claims 24 to 41 wherein the powdered medicament comprises a drug.

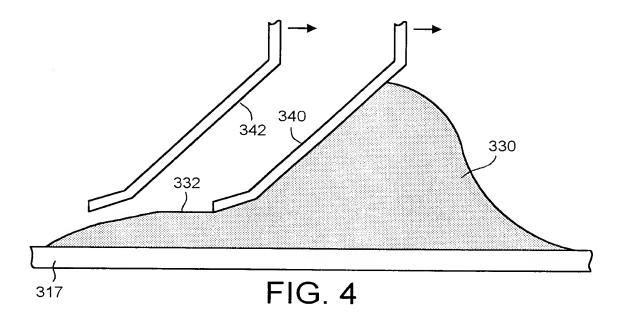
- 43. A method according to claim 42 wherein the drug is selected from the group consisting of albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof and any mixtures thereof.
- 44. A method according to either of claims 42 and 43 wherein the powdered medicament additionally comprises an excipient.
- 45. A method according to claim 44 wherein the excipient is a sugar.
- 46. Use of an apparatus according to any of claims 1 to 23 for densifying, preparing or levelling a sample of powdered medicament.

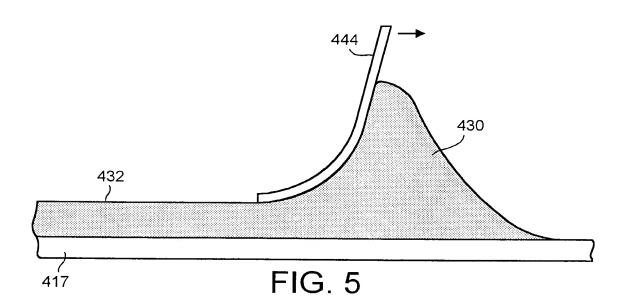












INTERNATIONAL SEARCH REPORT

In .ational Application No PCT/EP 00/04500

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 B65B63/02 B30B B30B15/30 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) B65B B30B Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Category 3 Relevant to claim No. GB 353 594 A (LEADLEY) 30 July 1931 (1931-07-30) χ 1,2, 11-13,15 page 2, line 105-110 WO 95 31239 A (CAMBRIDGE CONSULTANTS) Υ 1-3. 23 November 1995 (1995-11-23) 11 - 14. 19-26, 34 - 37, 42-46 page 1 page 13, paragraph 2; figure 7 US 3 656 518 A (ARONSON) Υ 1 - 3, 18 April 1972 (1972-04-18) 11-14. 19-26, 34 - 3742-46 column 18, line 15-26; figures 31,32 Further documents are listed in the continuation of box C. Patent family members are listed in annex. X Х Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled other means "P" document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 28/09/2000 1 September 2000 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Grentzius, W Fax: (+31-70) 340-3016

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